Asymmetricaly substituted calix[4]pyrrole with chiral substituents

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Supplementary material

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Experimental

TLC was performed on HF_{254} plates (Merck), detection by UV light or by spraying with a solution of 5 g of $Ce(SO_4)_2$ in 500 ml 10 % H_2SO_4 and subsequent heating. Flash column chromatography was performed on silica gel (MERCK, 100-160 μm) in solvents, distilled prior to use. Optical rotations were measured in $CHCl_3$ solutions on a Rudolph Research Autopol VI polarimeter at 25 °C and $[\alpha]_D$ values are given in 10^{-1} deg.cm^2.g^{-1} with concentration in 10 g.l^{-1}, unless stated otherwise. UV spectra were recorded on Specord 210 spectrometer (Analytik Jena) (with ε given in dm^3.cm^{-1}.mol^{-1}). IR spectra (wavenumbers in cm^{-1}) were recorded on a Perkin-Elmer PE 580 spectrometer in $CHCl_3$ solutions (temperature 23 °C), unless stated otherwise. ^1H and ^{13}C NMR spectra were taken in $CDCl_3$ (Aldrich, 99.8 %D) on a Bruker AVANCE 500 (500.1 MHz for ^1H and 125.8 MHz for ^{13}C) FT NMR spectrometer at 300 K if not stated otherwise. As standard the internal signal of tetramethylsilane (δ 0.0) for ^1H and central line of solvent (δ 77.0) for ^{13}C were used. Chemical shifts are presented in ppm (δ), coupling constants in Hz (J). Mass spectra were taken on a Q TOF micromass spectrometer with direct inlet (ESI) or on a ZAB-EQ (VG Analytical) instrument (FAB) with Xe ionization, accelerating voltage 8 kV.

All solvents used were of highest degree of purity and used as received. Calix[4]pyrroles solutions for spectroscopic studies have been prepared by using solvents of spectroscopic grade. Milli-Q, Millipore, previously doubly distilled water, was used for the preparation of porphyrin aqueous solutions.

5,6,7,9-Tetra-*O*-acetyl-4,8-anhydro-1,2,3-trideoxy-2',2''-di-1*H*-pyrrol-2-yl-D-*glycero*-D-*gulo*-nonitol 1

To a solution of pyrrole (2.9 ml, 42 mmol) and ketone **2** (ref.[11], 400 mg, 1.05 mmol) in 14 ml of dry CH_2Cl_2, was added trifluoroacetic acid (15 µl 0.2 mmol). The solution was stirred in the dark at ambient temperature under Ar for 20 hours. The reaction mixture was extracted with $NaHCO_3$, NH_4Cl, dried, the solvent was evaporated and residue was subjected to chromatography on silica gel (cyclohexane-ethyl acetate 4:1) to give the dipyrrole **1** (320 mg, 60 %); $[\alpha]_D$ + 3.0 (c 0.5); UV spectrum: λ_{max}(EtOH)/nm 209 (ε 5.9 × 10^{10}); IR spectrum: υmax/cm-1 -OAc: 1750vs, br; 1255vs, br; 1049s, sh; 1034vs; 599m; 1376vs; 1368vs; 1143m; 978m; 2-subst. pyrrole: 3459s; 3386m, br; 3105w; 1556m; 1415sh; ^1H NMR spectrum: δH (300 MHz) 1.62 (3H, s, H-1), 2.01-1.83(13H, m, H-3b, 4xCH_3CO), 2.35 (1H, m, H-3a), 3.16 (1H, dd, *J* = 8.7, *J* 8.9, H-4), 3.32 (1H, ddd, *J* = 1.8, *J* = 5.6, *J* 9.6, H-8), 3.90 (1H, dd, *J* = 1.8, *J* = 12.2, H-9b), 4.03 (1H, dd, *J* = 5.6, *J* = 12.2, H-9a), 4.81 (1H, dd, *J* = 9.3, *J* = 9.5, H-5), 4.89 (1H, dd, *J* = 9.5, *J* = 9.5, H-7), 4.98 (1H, dd, *J* = 9.1, *J* = 9.1, H-6), 6.06-5.93 (4H, m, H-4', H-4'', H-3', H-3''), 6,45 (1H, d, H-5''), 6.51 (1H, d, *J* = 1.3, H-5'), 7.78 (1H, bs, H-NH), 8.01 (1H, bs, H-NH); ^{13}C NMR spectrum δC (75 MHz) 21.0, 21.0, 21.1, 21.1 (4xCH_3CO), 28.3 (C-1), 38.9 (C-2), 42.5 (C-3), 62.9 (C-9), 69.0 (C-7), 72.1 (C-5), 74.8 (C-6), 76.7 (C-8), 76.0 (C-4), 104.8 (C-5´´), 105.9 (C-4´), 108.1 (C-3''), 108.2 (C-3'), 117.4 (C-5''), 117.7 (C-5'), 137.0 (C-2''), 138.0 (C-2'), 169.9, 170.2, 170.7, 171.1 (4xCH_3CO); For $C_{25}H_{32}N_2O_9$ (504.52) calculated monoisotopic mass: *m/z* 504.210781 found: (TOF/ES+) 527.2005 $[M+Na]^+$. Found: C, 59.7; H, 6.2; N, 5.4. $C_{25}H_{32}N_2O_9$ requires C, 59.5; H, 6.4; N, 5.55%.

3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-1-deoxy-1--(5,10,10,15,15,20,20-heptamethyl-5,10,15,20,22,24--hexahydroporphyrin-5-yl)-D-*glycero*-D-*gulo*-heptitol 4

and a mixture of

5,10-*cis* and *trans* 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-1-deoxy--1-(5,10,15,15,20,20-heptamethyl-5,10,15,20,22,24-hexahydro-porphyrin-5,10-diyl)-bis-D-*glycero*-D-*gulo*-heptitols 3

To a solution of dipyrrylmethane **1** (200 mg, 0.39 mmol) in 16 ml of dry CH_2Cl_2 was added acetone (44 µl, 0.6 mmol). Then trifluoroacetic acid (5 µl, 0.07 mmol) was added as catalyst. The reaction vessel was shielded from light and stirring under Ar at ambient temperature for one night then acetone (44 µl, 0.6 mmol) and trifluoroacetic acid (5 µl, 0.06 mmol) and the reaction mixture was stirred for additional night. Then the Et_3N (15 µl, 0.1 mmol) and silica gel were added and the solvent was evaporated under vacuum. The resulting powder was posed at the top of a short silica gel column. Increasing polarity elution with cyclohexane:ethylacetate 6:1→4:1 gave derivative **4** (50 mg, 16 %) in the first major fraction.

$[\alpha]_D$ - 3.6 (c 0.25). UV spectrum: λ_{max}(EtOH)/nm 210 (ε 8.07 × 10^{10}). IR spectrum: -OAc: 1752vs; 1710m, sh; 1254s, sh; 1230vs; 1041m; 1033m, sh; 600w; 1376m; 1367m; 1144w; 977w; pyrrole: 3438m; 3111w; 1576w; 1501w; 1417m; gem. Me2: 2973m; 1383m, sh; 1367m. ^1H NMR (300 MHz): δ (ppm) 7.03 (bs, 2H, H-NH); 6.96 (bs, 2H, H-NH); 5.88-5.73 (m, 8H, Hβ-pyrrole); 4.97 (dd, 1H, *J* = 9.2 Hz, J = 8.8 Hz, H-7); 4.91 (dd, 1H, *J* = 10.8 Hz, *J* = 9.3 Hz, H-6); 4.81 (dd, 1H, *J* = 9.7 Hz, *J* = 8.9 Hz, H-5); 4.03 (dd, 1H, *J* = 5.12 Hz, *J* = 12.2 Hz, H-9a); 3.81 (dd, 1H, *J* = 2.2 Hz, *J* = 12.2 Hz, H-9b);

3.35-3.30 (m, 1H, H-8); 3.09 (dd, 1H, *J* = 8.9 Hz, J = 9.1 Hz, H-4); 2.05 (m, 1H, H-3a), 1.99, 1.94, 1.92, 1.91 (4xs, 12H, $4xCH_3CO$); 1.80 (m, 1H, H-3b); 1.44-1.41 (7xs, 21H, H-1, H-CH_3). ^{13}C NMR (75 MHz): δ (ppm) 171.04, 170.83, 170.09, 169.91 ($4xCH_3CO$), 139.61, 139.10, 138.87, 138.74, 138.68, 137.55, 136.01 (Cα-pyrrole); 105.34, 103.64, 103.38, 103.33, 103.27, 103.12, 103.02 (Cβ-pyrrole); 75.85 (C-7); 75.58 (C-8); 74.95 (C-4); 71.99 (C-5); 69.02 (C-6); 62.73 (C-9); 41.51 (C-3); 35.59, 35.56 (C-2, Cquat.); 29.97, 29.66, 29.39, 27.63, 27.29, 23.08 (C-1); 21.16, 21.06, 21.00 ($4xCH_3CO$). For $C_{42}H_{54}N_4O_9$, (758.90) calculated monoisotopic mass: 758.389079; found: MS (FAB), *m/z*: 791.4 $[M+MeOH]^+$ HRMS (TOF/ES+), *m/z*: 759.3969 $[M+H]^+$. Found: C, 66.6; H, 7.0; N, 7.6. $C_{42}H_{54}N_4O_9$ requires C, 66.5; H, 7.2; N, 7.4%.

Further elution of the above column gave amorphous mixture of isomers **3** (70 mg, 16 %).

UV spectrum: λ_{max}(EtOH)/nm 210 (ε 1.02 × 10^{11}). IR spectrum: -OAc: 1752vs, br; 1251vs, br; 1043vs, sh; 1034vs; 600m; 1375s; 1368vs; 1143m; 978m; pyrrole: 3437m; 3378m; 3111w; 1575m; 1495w, br, sh; 1419m; gem. Me_2: 2975s; 1388s, sh; 1368vs. ^{1}H NMR (300 MHz): δ (ppm) 7.09-6.91 (m, 4H, H-NH); 5.89-5.71 (m, 8H, Hβ-pyrrole); 5.05-4.72 (m, 6H, H-sugar moiety); 4.14-3.58 (m, 4H, H-sugar moiety); 3.44-2.93 (m, 4H, H-sugar moiety); 2.11-1.63 (m, 20H, H-3a, H-3b, 24H, $4xCH_3CO$); 1.52-1.29 (m, 6xH-CH_3). ^{13}C NMR (75 MHz): δ (ppm) 170.89, 170.69, 170.62, 170.50, 169.87, 169.81, 169.75, 169.63, 169.58, 169.47 (CH_3CO), 139.35, 139.26, 139.20, 138.60, 137.99, 137.76, 137.30, 137.12, 135.81, 135.63, 135.39, 134.95 (Cα-pyrrole); 105.65, 105.11, 104.88, 104.00, 103.62, 103.33, 103.19, 103.11, 103.01, 102.48 (Cβ-pyrrole); 76.74, 75.59, 75.52, 75.30, 74.75, 74.60, 74.50, 72.16, 71.65, 71.54, 69.00, 68.75, 68.61, 68.23 (C-sugar moiety); 42.68, 41.90, 41.37, 41.03 (C-3); 38.69, 38.46, 38.41, 37.96, 35.36, 35.30 (C-2, Cquat.); 30.45, 29.88, 29.74, 29.62, 29.48, 29.29, 29.20, 28.99, 28.22, 27.58, 27.28 (C-1, C-CH_3); 21.14, 21.03, 20.98 ($4xCH_3CO$). For ($C_{56}H_{72}N_4O_{18}$, 1189.19) calculated monoisotopic mass 1088.484161, found MS (FAB) *m/z*: 1089.54 $[M]^+$ HRMS (TOF/ES+), *m/z*: 1089.4920 $[M+H]^+$. Found: C, 62.0; H, 6.5; N, 5.4. $C_{56}H_{72}N_4O_{18}$ requires C, 61.75; H, 6.7; N, 5.1%.

4,8-anhydro-1,2,3-trideoxy-2',2''-di-1*H*-pyrrol-2-yl-D-*glycero*-D-*gulo*-nonitol 6

To a solution of pyrrole (1.6 ml, 23.2 mmol) and ketone **5** (ref.[12], 990 mg, 4.5 mmol) in 15 ml of dry methanol (25 µl, 0.4 mmol) of methanesulfonic acid was added and a solution was stirred in the dark at ambient temperature under Ar for 2 days. The reaction was quenched by addition of a (40 µl, 0.5 mmol) pyridine.

The mixture was concentrated and the crude product was purified by chromatography (chlorofom/methanol 4:1) to give of dipyrrylmethane **6** (910 mg, 60 %) as white foam.

$[\alpha]_D$ + 218.3 (c 0.1). ^{1}H NMR (CD_3OD): δ (ppm) 9.72 (bs, 1H, H-NH); 9.55 (bs, 1H, H-NH); 6.60 (dd, 1H, *J* = 2.5 Hz, *J* = 1.4 Hz, H-5'); 6.58 (dd, 1H, *J* = 2.2 Hz, *J* = 1.2 Hz, H-5''); 5.96 (dd, 1H, *J* = 3.0 Hz, *J* = 2.9 Hz, H-4'); 5.94 (dd, 1H, *J* = 2.9 Hz, *J* = 2.8 Hz, H-4''); 5.92 (m, 1H, H-3'), 5.88 (m, 1H, H-3''); 3.74 (dd, 1H, *J* = 2.2 Hz, *J* = 11.6 Hz, H-9a); 3.46 (dd, 1H, *J* = 6.8 Hz, *J* = 11.6 Hz, H-9b); 3.35-3.18 (m, 3H, H-8, H-7, H-6); 3.11-3.03 (m, 2H, H-4, H-5); 2.98 (dt, 1H, *J* = 2.3 Hz, *J* = 6.9 Hz, H-8); 2.57 (d, 1H, *J* = 14.5 Hz, H-3a); 2.03 (dd, 1H, *J* = 8.5 Hz, *J* = 14.6 Hz, H-3b); 1.67 (s, 3H, H-1). ^{13}C NMR (CD_3OD): δ (ppm) 140.23 (C-2'); 139.41 (C-2''); 117.58 (C-5'); 117.43 (C-5''); 108.25 (C-4'); 108.19 (C-4''); 105.49 (C-3'); 104.84 (C-3''); 81.19 (C-8); 79.88 (C-6); 78.73 (C-5); 75.60 (C-4); 72.22 (C-7); 63.39 (C-9); 44.01 (C-3); 39.74 (C-2); 28.40 (C-1). For $C_{17}H_{24}N_2O_5$, (336.38) calculated monoisotopic mass 337.168522; found HRMS (FAB), *m/z*: 337.175438 $[M]^+$. Found: C, 60.9; H, 7.15; N, 8.4. $C_{17}H_{24}N_2O_5$ requires C, 60.7; H, 7.2; N, 8.3%

5,5,10,10,15,15,20-(heptamethyl)-20-(2',6'-anhydro-1'-deoxy-D-*glycero*-D-*gulo*-heptitol-1'-yl)calix[4]pyrrole 7

Reaction A: To a solution of dipyrrylmethane **6** (400 mg, 1.19 mmol) in 50 ml of dry methanol was added acetone (320 µl, 4.36 mmol). Then methanesulfonic acid (27 µl, 0.35 mmol) was added as catalyst. The reaction vessel was shielded from light and stirring was continued for 3 hours under Ar at ambient temperature. Then pyridine (40 µl, 0.5 mmol) and silica gel were added and the solvent was evaporated under vacuum. The resulting powder was posed at the top of a short silica gel column. Increasing polarity elution with $CHCl_3$, $CHCl_3$/MeOH 4:1 gave product 7 (80 mg, 11 %) as white solid.

Reaction B: To a solution of dipyrrylderivative **8** (120 mg, 0.68 mmol) in 3 ml of dry methanol was added carbohydrate derivative 5 (150 mg, 0.68 mmol). Then methanesulfonic acid (6 µl, 0.08 mmol) was added as catalyst. The reaction vessel was shielded from light and stirring was continued for 24 hours under Ar at ambient temperature. Then the pyridine (9 µl, 0.74 mmol) and silica gel were added and the solvent was evaporated under vacuum. The resulting powder was posed at the top of a short silica gel column. Increasing polarity elution with $CHCl_3$, $CHCl_3$/MeOH 4:1 gave product **7** (10 mg, 10 %) as white amorphous solid as above ad A/.

$[\alpha]_D$ + 86.3 (c 0.09). UV spectrum λ_{max}(EtOH)/nm 209 (ε 6.9 × 10^{10}). IR spectrum: 3114m (=CH); ring: 1576m, 1510m, 1416s; gem. Me_2: 2976s, 1385s, 1363s. ^{1}H NMR: δ (ppm) 8.20 (bs, 1H, H-NH); 8.18 (bs, 1H, H-NH); 8.03 (bs, 1H, H-NH); 7.99 (bs, 1H, H-NH); 5.99-5.72 (m, 8H, H-pyrrole); 3.67 (d, 1H, *J* = 11.4 Hz, H-7'a); 3.44 (dd, 1H, *J* = 11.4 Hz, *J* = 6.3 Hz, H-7'b); 3.25-2.95 (m, 5H, H-6', H-5', H-4', H-3', H-2'); 2.47 (d, 1H, *J* = 14.4 Hz, H-1'a); 1.98 (dd, 1H, *J* = 14.5 Hz, *J* = 7.2 Hz, H-1'b); 1.65-1.48 (m, 21H, H-CH_3). ^{13}C NMR: δ (ppm) 140.37, 140.22-140.04, 139.81, 138.80 (C-Cα pyrrole); 140.96, 103.67-103.23 (C-CH pyrrole); 81.02, 79.88, 78.51, 75.44, 72.13 (C-2', C-3', C-4', C-5', C-6'); 63.42 (C-7'); 43.14 (C-1'); 36.42-36.34 (C-meso); 30.01-29.72 (C-CH_3); 28.04 (C-CH_3). For $C_{34}H_{47}N_4O_5$ (590.75) calculated monoisotopic mass 590.346821; found HRMS (FAB), *m/z*: 591.355115 $[M+H]^+$. Found: C, 69.3; H, 7.7; N, 9.5. $C_{34}H_{46}N_4O_5$ requires C, 69.1; H, 7.85; N, 9.5%

Notes and references

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